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Abstract

Seventy-one cases of bronchial asthma were classified into three types: bronchospasm, bronchospasm-hypersecretion and bronchiolar obstruction types. The characteristics of each type were studied in relation to patient age and age at onset of the disease. In the 71 subjects studied, the most frequent type was the bronchospasm type followed by the bronchospasm-hypersecretion type and bronchiolar obstruction type. Intractable asthma was most frequently observed in the bronchiolar obstruction type and least in the bronchospasm type. Most of the patients under 50 years of age showed the bronchospasm type. The bronchospasm-hypersecretion type was characteristically accompanied by blood eosinophilia when the patient age was under 50 years. In the bronchospasm-hypersecretion type, the incidence of intractable asthma was high in patients under 50 years of age, but not remarkable in those over 50. A large proportion of the patients over 50 years of age were of the bronchiolar obstruction type. There was no difference in the incidence of intractable asthma between the two groups classified by age at onset.

KEYWORDS: asthma classification, clinical symptoms, patient age, age at onset

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CLASSIFICATION OF ASTHMA BASED ON CLINICAL SYMPTOMS : ASTHMA TYPE IN RELATION TO PATIENT AGE AND AGE AT ONSET OF DISEASE

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Abstract. Seventy-one cases of bronchial asthma were classified into three types: bronchospasm, bronchospasm-hypersecretion and bronchiolar obstruction types. The characteristics of each type were studied in relation to patient age and age at onset of the disease. In the 71 subjects studied, the most frequent type was the bronchospasm type followed by the bronchospasm-hypersecretion type and bronchiolar obstruction type. Intractable asthma was most frequently observed in the bronchiolar obstruction type and least in the bronchospasm type. Most of the patients under 50 years of age showed the bronchospasm type. The bronchospasm-hypersecretion type was characteristically accompanied by blood eosinophilia when the patient age was under 50 years. In the bronchospasm-hypersecretion type, the incidence of intractable asthma was high in patients under 50 years of age, but not remarkable in those over 50. A large proportion of the patients over 50 years of age were of the bronchiolar obstruction type. There was no difference in the incidence of intractable asthma between the two groups classified by age at onset.

Key words : asthma classification, clinical symptoms, patient age, age at onset.

Bronchial asthma is a chronic, obstructive lung disease in which bronchospasm is induced by increased responsiveness of the trachea and bronchi to various stimuli. The pathogenetic mechanism is complicated, and there are still many unexplainable points. Bronchial asthma is usually classified into two types: extrinsic and intrinsic asthma. In extrinsic asthma an IgE antibody (1, 2) is produced against an antigen existing outside, and an attack of asthma is induced by the reaction with the IgE antibody. However, the pathogenesis of intrinsic asthma has not been elucidated. Swineford (3) classified bronchial asthma into three types: atopic-, infectious- and mixed-type. The atopic type is almost the same as extrinsic asthma. It is difficult, however, to understand infectious- and mixed-type asthma precisely. At the present time, there is no available classification of bronchial asthma according to clinical features, treatment and prognosis.

In this study, bronchial asthma is classified according to the clinical findings

and examined in relation to patient age, age at onset of the disease and severity of the disease. The pathogenetic mechanism is discussed.

SUBJECTS AND METHODS

Included in the study were 71 patients, 42 females and 29 males, with bronchial asthma. Their mean age was 45.8 years (ranging from 16 to 71 years), and their mean age at onset of the disease was 32.2 years (between 4 and 61 years). Among these subjects, 24 were steroid-dependent, severely intractable asthma patients having suffered for one year or longer.

Pathophysiological classification. The subjects were classified into three types: 1-a, bronchospasm type; 1-b, bronchospasm + hypersecretion type, and 2, bronchiolar obstruction type, according to the clinical findings. In the bronchospasm type, the attacks were mainly due to bronchospasm. In the bronchospasm + hypersecretion type, attacks were accompanied by bronchospasm and hypersecretion (sputum of 100 ml or more/day). In the bronchiolar obstruction type, attacks were related to the obstruction of the bronchiole as well as to bronchospasm. For diagnosis of the bronchiolar obstruction type, we referred primarily to the stethoscopic findings *i.e.*, transient bubbling rales mainly at the lower fields of the lung, weakening or disappearance of breath sounds and relatively unremarkable dry rales or prolongation of expiration. Clinically, attacks of asthma of this type included features such as unremarkable wheezing, gradual potentiation of asthma attacks for several days after an upper air-way infection and high degree of dyspnea.

Histamine release from basophils. The whole blood method (4) was employed, as previously described (5). Tubes containing 4 ml of heparinized venous blood were incubated at 37°C for 15 min after 0.2 ml of anti-human IgE (Behringwerke) was added. The tubes were put into ice water to terminate the reaction, and the supernatant and cell pellet were divided by centrifugation at $400 \times g$ for 20 min at 4°C. The amount of histamine released was determined by an automated histamine analysis system (6, 7). The results were expressed as a percentage of the total histamine content. All drugs for treatment were stopped for 12 h prior to determining histamine release.

Total serum IgE was measured by a RIST method.

RESULTS

The distribution of the 71 cases of bronchial asthma was: 38 cases (53.5 %) of type 1-a (bronchospasm type), 23 cases (32.4 %) of type 1-b (bronchospasm-hypersecretion type) and 10 cases (14.0 %) of type 2 (bronchiolar obstruction type). Four cases (10.5 %) of the 38 type 1-a cases, 12 cases (52.2 %) of the 23 type 1-b cases and 8 cases (80 %) of the 10 type 2 cases were of severe intractable asthma. Thus, severe intractable asthma appeared most frequently in type 2, followed by type 1-b and type 1-a (Fig. 1).

Patient age and type of asthma. The subjects were divided by age into two groups: patients under 50 years of age and patients over 50 years of age, and the incidence of each type was compared.

Twenty-eight (73.7 %) of the 38 cases of type 1-a, 12 (52.2 %) of the 23 cases of type 1-b and one (10.0 %) of the 10 cases of type 2 belonged to the group of the patients under 50 years of age. The result indicated that the bronchospasm

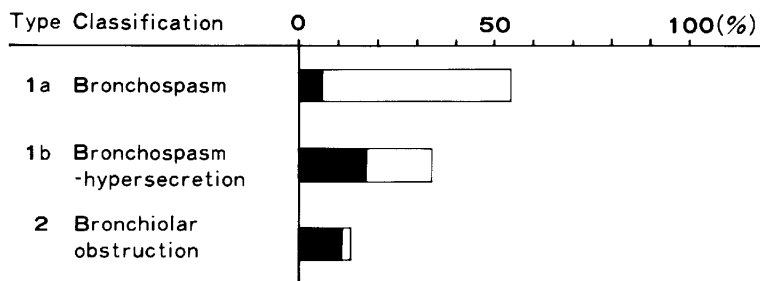


Fig. 1. Asthma classification based on clinical findings and the incidence of each asthma type among all patients studied. ■ : Intractable asthma.

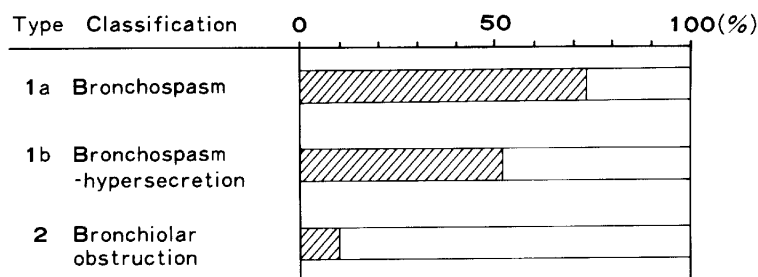


Fig. 2. Asthma classification and patient age. ▨ : Patients under 50 years of age, □ : Patients 50 years of age or over.

type appears most often in patients under 50. The bronchiolar obstruction type, however, appeared frequently in the patients over 50 years of age. There was no significant difference in the incidence of bronchospasm-hypersecretion type between the two age groups (Fig. 2).

The serum IgE level in patients of each type was compared between the two age groups. The serum IgE was 920 ± 273 IU/ml (mean \pm SEM) in the patients under 50 years of age, and 253 ± 29 IU/ml in those over 50 in type 1-a. In type 1-b, it was 212 ± 32 IU/ml in patients under 50, 190 ± 36 IU/ml in those over 50, and in type 2, 212 ± 15 IU/ml in the patients over 50. The serum IgE was significantly high only in the patients under 50 years of age in type 1-a (Fig. 3).

The peripheral eosinophil count (%) was 8.9 ± 0.7 % in the patients under 50 years of age and 6.1 ± 1.4 % in those over 50 in type 1-a, and there was no significant difference between the two groups. In type 1-b, it was 12.7 ± 2.0 % in the patients under 50 and 5.6 ± 1.2 % in those over 50. A significant difference in the eosinophil count was present between the two groups in type 1-b ($p < 0.01$). It was 4.8 ± 1.4 % in the patients over 50 in type 2. These results indicate a considerable correlation between bronchial hypersecretion and the in-

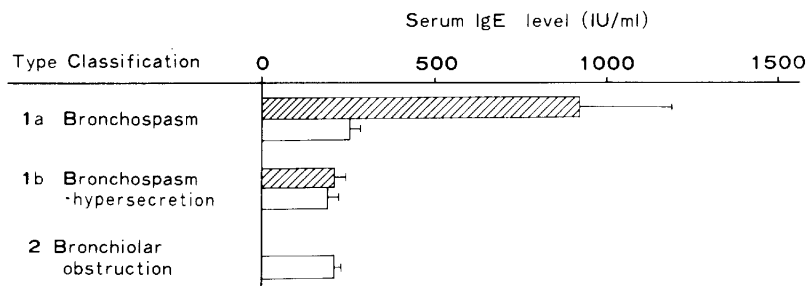


Fig. 3. Concentration of serum IgE in each asthma type. : Patients under 50 years of age, : Patients 50 or over.

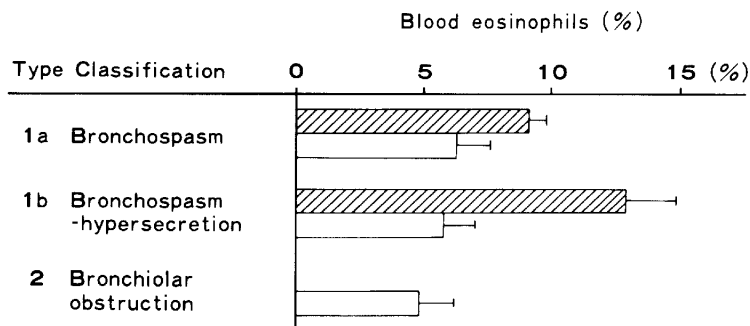


Fig. 4. Blood eosinophil count in each asthma type. : Patients under 50 years of age, : Patients 50 or over.

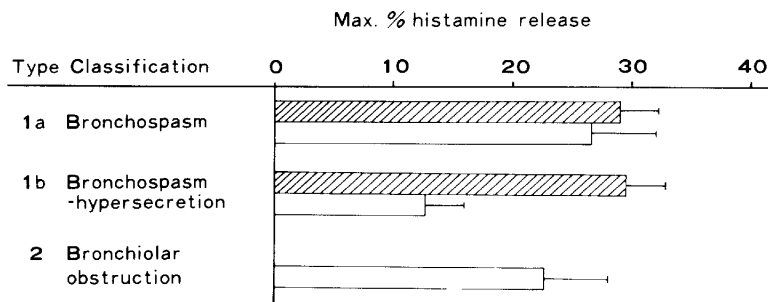


Fig. 5. Maximum percent histamine release from whole blood induced by anti-IgE in each asthma type. : Patients under 50 years of age, : Patients 50 or over.

crease in the peripheral eosinophil count in patients under 50 years of age (Fig. 4).

Histamine release from basophils after addition of anti-human IgE was deter-

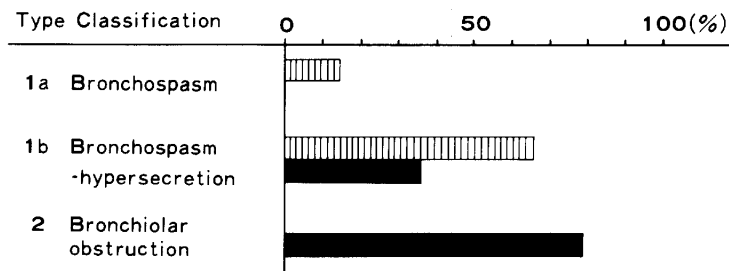


Fig. 6. Incidence of intractable asthma in each asthma type and patient age. ▨ : Patients under 50 years of age, ■ : Patients 50 or over.

mined in the two age groups in each type. It was $29.2 \pm 3.2\%$ in the patients under 50 years of age and $26.7 \pm 5.5\%$ in those over 50 in type 1-a. There was no significant difference between the two groups. In type 1-b, it was $29.8 \pm 3.2\%$ and $12.8 \pm 3.4\%$. Significantly greater histamine release was observed in the patients under 50 in type 1-b than in the patients over 50 ($p < 0.01$). This evidence suggests that the pathophysiological mechanisms participating in the attacks of the patients under 50 differ from those of the patients over 50 in type 1-b (Fig. 5).

The incidence of intractable asthma in each type was studied in relation to patient age. The incidence of intractable asthma was 14.3% (4/28) in the patients under 50 years of age in type 1-a. In type 1-b, such cases were 66.7% (8/12) in the patients under 50 and 36.4% (4/11) in those over 50. A higher incidence of intractable asthma was observed in the patients under 50 in type 1-b, although there was no statistically significant difference between them. All the intractable asthma patients in type 2 were over 50, and the incidence was 80% (8/10). These results show that the severity of asthma is potentiated by the co-existence of hypersecretion with bronchospasm in the patients under 50 years of age (Fig. 6).

Age at onset and type of asthma. The subjects were divided into two groups according to the age at onset of the disease: those under 40 years of age and those over 40, namely, 'late onset' asthma. There were 27 (71.0%) patients under 40 years of age at the onset of bronchial asthma in the 38 cases of type 1-a, 10 (43.5%) in the 23 cases of type 1-b and 3 (30.0%) in the 10 cases of type 2. The majority of type 1-a patients were under 40 years of age at onset, and the majority of bronchiolar obstruction type patients were over 40 years of age at onset. The incidence of type 1-b was almost the same in the two onset age groups (Fig. 7). All the intractable asthma patients in type 1-a were under 40 at onset. In type 1-b, intractable asthma was seen in 6 (60.0%) of the 10 cases in the group under 40. Intractable asthma appeared slightly more frequently in the younger age at onset group in type 1-b, though there was no signi-

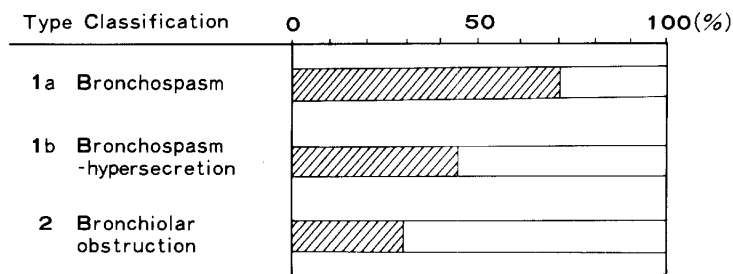


Fig. 7. Asthma classification and age at onset of disease. : Patients less than 40 years of age at onset, : Patients 40 or over at onset of disease.

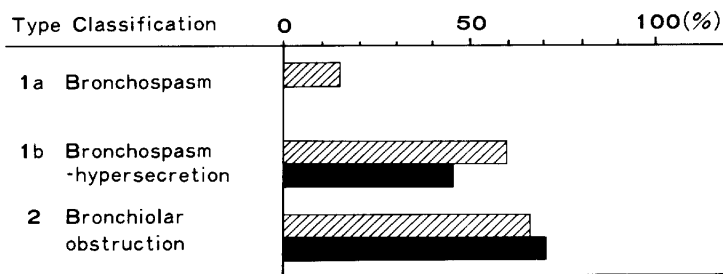


Fig. 8. Incidence of intractable asthma in each asthma type and age at onset of disease. : Patients less than 40 years of age at onset, : Patients 40 or over at onset of disease.

ficant difference between the two onset age groups. In type 2, intractable asthma was seen in 2 (66.7 %) of the 3 patients who were under 40 years of age at onset and in 5 (71.4 %) of the 7 patients who were over 40 at onset. Intractable asthma appeared with considerably high incidence in both groups in this type (Fig. 8).

DISCUSSION

The pathogenetic mechanism of bronchial asthma is so complicated and includes so many factors that there are still many unexplainable points. Particularly, late onset asthma (8, 9), appearing in patients over 40 years old, is considerably different from atopic asthma which is related to immediate-type allergic reactions caused by IgE. This fact suggests that clinical features of bronchial asthma are considerably influenced by the age of patients and their age at onset of the disease (10).

In the present study, bronchial asthma was classified into three types: bronchospasm type, bronchospasm-hypersecretion type and bronchiolar obstruction type, according to clinical symptoms, and the features were compared in relation to patient age and age at onset of the disease. When patients were divided into

two groups, those under 50 and those over 50 years of age, it was found that the majority of type 1-a (bronchospasm type) patients were under 50. In patients of both groups, the serum IgE level was high and the histamine release from basophils induced by anti-IgE was remarkable. These results suggest that the IgE-mediated reaction plays an important role in type 1-a. In type 1-b (bronchospasm-hypersecretion type) there were many patients under 50 years of age, and there was an increase in the peripheral eosinophil count. In these patients, histamine release induced by anti-IgE was remarkable and the incidence of intractable asthma was high, while, in type 1-b patients over 50 years old, an increase in the peripheral eosinophil count was rare, the histamine release from basophils was not remarkable and the incidence of intractable asthma did not appear frequently. This result indicates that aging influences the pathogenetic mechanism in type 1-b, and it was characteristic that bronchial hypersecretion in the patients under 50 was accompanied by blood eosinophilia. Almost all the cases of type 2 (bronchiolar obstruction type) were observed in patients over 50 years old. The age at onset scarcely caused any change in type 2, suggesting that changes with aging are a considerably important factor. Consequently, these three types of bronchial asthma with different clinical symptoms are influenced by the type and strength of allergic reactions involved and by changes in aging, and correlate closely to the prognosis.

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